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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/987,763

Applicant(s)

CRAFTON ET AL.

Examiner

Sumesh Kaushal

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-22 and 24-73 is/are pending in the application.
- 4a) Of the above claim(s) 39-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-22 and 24-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response filed on 12/10/04 has been acknowledged.

Claims 1-73 are pending.

Claims 2 and 23 are canceled

Claims 1-2, 4-22 and 24-38 are examined in this office action.

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Election/Restrictions

Applicant's election without traverse of Group IV claims 1-38 (*wherein the elected subject matter is nucleotides sequences of **SEQ ID NO: 7** and **dihydrodipicolinate reductase***) in the reply filed on 06/18/04 was acknowledged, in the office action mailed on 10/04/04.

This application contains claims 39-73 drawn to an invention nonelected with traverse in Paper No. 06/18/04. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 101

Claims 1-2, 4-22 and 24-38 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well-established utility for the same reasons of record as set forth in the office action mailed on 10/04/04.

The instant claims are drawn to an isolated DNA sequence (SEQ ID NO:7) or any variant thereof that is capable of regulating the transcription of a gene or interest. table-1A). However the specification as filed fails to disclose that nucleic acid sequences of SEQ ID NO:7 is a regulatory sequence that regulates transcription of a gene of interest in general or in response to pyruvate.

The

The instant invention is not considered to have a specific and/or substantial utility, since the instant specification fails to establish that that the disclosed polynucleotide sequence (SE ID NO:7) is a transcription regulatory element explicitly or implicitly as putatively considered by the instant specification. The asserted transcription activity is mere computer-generated hypotheses, since no biological function has been established. The specification fails to disclose a functional assay that would enable one skill in the art how to evaluate the biological activity of the regulatory element encoded by SEQ ID NO:7. In addition the specification fails to establish any nexus between pyruvate metabolism and a regulatory element encoded by SEQ ID NO:7. Considering the applicant's disclosure, it is unclear whether pyruvate would up-regulate or down-regulate the transcription a gene operatively linked to the nucleic acid sequences of SEQ ID NO:7. The official sequence search using the disclosed nucleic acid sequences fails to provide any evidence that the polynucleotides of SEQ ID NO:7 is transcriptional regulatory element that is responsive to pyruvate.

In addition, the scope of invention as claimed encompasses any and all variants of nucleotide sequence of SEQ ID NO:7 that encodes any or a pyruvate responsive transcriptional element. The variations as claimed encompasses conserved motifs that are considered germane to the pyruvate responsive transcriptional activity. It is general knowledge in the art that even conservative nucleotide substitutions can adversely affect the transcriptional site and corresponding biological activity if nucleic acids sequences that are critical for such functions are substituted, added or deleted. see Ngo, in *The Protein Folding Problem and Tertiary Structure Prediction*, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in *Peptide Hormones*, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). The specification even fails to define what comprises the minimal structure or

Art Unit: 1636

consensus core structure that defines the functional domain of the regulatory element present in the nucleic acid sequences of SEQ ID NO:7. In view of the foregoing, one skilled in the art would not readily attribute that the nucleic acid sequence or any variant thereof as claimed is a pyruvate responsive transcriptional element. Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the nucleic acid sequence as claimed. The only immediate apparent utility for the instant invention would be further scientific characterization of the claimed nucleic acid sequences a putative pyruvate responsive transcriptional element.

Response to arguments

The applicant argues that only one credible assertion of utility is necessary. The applicant argues that claim 2 states that the claimed polynucleotide regulates transcription of β -galactosidase in a bacterial host cell. The applicant argues that the increased expression of β -galactosidase under the transcriptional control of SEQ ID NO:7 is shown in Table 9 and discussed in example 9. The applicant argues that β -galactosidase is recognized as an enzyme that cleaves lactose into galactose and glucose.

However, applicant's arguments are found NOT persuasive. As stated earlier the instant invention is not considered to have a specific and/or substantial utility, since the the specification as filed fails to establish that that the disclosed polynucleotide sequence (SEQ ID NO:7) is a transcription regulatory element explicitly or implicitly as putatively considered by the instant specification. Even the specification asserts that the SEQ ID NO:7 encodes a *Ldh* like responsive element that is regulated by pyruvate, the specification as filed fails to disclose that nucleic acid sequences of SEQ ID NO:7 capable of regulating the transcription of a reporter gene in response to pyruvate (see table 1A). Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the nucleic acid sequence as claimed. The only immediate apparent utility for the instant

invention would be further scientific characterization of the claimed nucleic acid sequences a putative pyruvate responsive transcriptional element.

Claim Rejections - 35 USC § 112

Claims 1-2, 4-22 and 24-38 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, for the same reasons of record as set forth in the office action mailed on 10/04/04.

Nature Of Invention:

Invention relates to a DNA sequence that regulates transcription of a gene operatively linked to the DNA sequence

Breadth Of Claims And Guidance Provided By The Inventor:

The instant claims are drawn to an isolated DNA sequence (SEQ ID NO:7) or any variant thereof that is capable of regulating the transcription of a gene or interest. In addition the claims are further drawn to expression vector and host cells comprising the claimed nucleic acid sequence or any variant thereof.

The specification asserts that the nucleic acid sequence of SEQ ID NO:7 is a putative gene identified by sequence homology that is responsive to putative regulatory molecule like pyruvate (Spec. page 23 table-1A). However the specification as filed fails to disclose that nucleic acid sequences of SEQ ID NO:7 is a regulatory sequence that regulates transcription of a gene of interest in general or in response to pyruvate.

The instant specification fails to establish that that the disclosed polynucleotide sequences (SE ID NO:7) is a transcription regulatory element explicitly or implicitly as putatively considered by the instant specification. The asserted transcription activity is mere hypotheses base upon sequence comparison, since no biological function has been established. The specification fails to disclose any functional assay that would enable one skill in the art how to evaluate the biological activity of the regulatory

Art Unit: 1636

element encoded by SEQ ID NO:7. In addition the specification fails to establish any nexus between pyruvate metabolism and the regulatory element encoded by SEQ ID NO:7. Considering the applicant's disclosure it is unclear whether pyruvate would up-regulate or down-regulate the transcription a gene operatively linked to the nucleic acid sequences of SEQ ID NO:7. The official sequence search using the disclosed nucleic acid sequences fails to provide any evidence that the polynucleotides of SEQ ID NO:7 is transcriptional regulatory element that is responsive to pyruvate.

In addition, the scope of invention as claimed encompasses any and all variants of nucleotide sequences that encode a pyruvate responsive transcriptional element. The variations as claimed encompasses the conserved motifs that are germane to the pyruvate responsive transcriptional activity. It is general knowledge in the art that even conservative nucleotide substitutions can adversely affect the transcriptional site and corresponding biological activity if nucleic acids sequences that are critical for such functions are substituted, added or deleted (*supra*). Furthermore making and testing a point mutation is significantly different from the making and testing nucleic acid sequences wherein unknown number of nucleotides are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. In the instant case the specification even fails to disclose a functional assay that would enable one skill in the art how to evaluate the biological activity of the regulatory element encoded by SEQ ID NO:7. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the proposed transcriptional and/or functional activity. In addition determining biological activity of a transcriptional elements base upon sequence similarity alone is not considered routine in the art and without sufficient guidance to a specific transcriptional motif and a functional assay experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in

Art Unit: 1636

support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to practice the invention as claimed. The quantity of experimentation required would include the functional characterization of polynucleotides of SEQ ID NO: 7 as a transcriptional regulatory element that is responsive pyruvate.

Response to argument

The applicant argues that, since the invention as claimed has specific and well-asserted utility the invention as claimed is fully enabled.

However, applicant's arguments are found NOT persuasive for the reasons of record and as stated above that invention as claimed lacks a specific asserted utility or a well-established utility. Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to practice the invention as claimed. For example, the specification as filed fails to disclose that an isolated polynucleotide comprising any 10 contiguous nucleotide of SEQ ID NO:7 is capable of regulating the transcription of a reporter gene in response to pyruvate. Therefore the undue experimentation required would include the functional characterization of polynucleotides of SEQ ID NO: 7 as a transcriptional regulatory element that is responsive pyruvate.

Claims 1-2, 4-22 and 24-38 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the office action mailed on 10/04/04.

The scope of invention as claimed encompasses any and all variants of SEQ ID NO:7, wherein the variant comprises a nucleic acid sequence which is 90% identical to SEQ ID NO:7 or a nucleic acid sequence that hybridizes SEQ ID NO:7.

At best the specification discloses only SEQ ID NO:7 but fails to disclose any variant of SEQ ID NO:7 that is capable of regulating the transcription of a gene of interest especially in the presence pyruvate. The scope of invention as claimed encompasses substitution, addition and/or deletion of at least 10% of nucleic acid sequences in the nucleic acid of SEQ ID NO:7. The specification fails to disclose any variant of SEQ ID NO:7 explicitly or implicitly that is capable of regulating the transcription of a gene of interest. The specification even fails to establish that nucleic acid sequence of SEQ ID NO:7 is a transcriptional element which is capable of regulating the expression of a gene in native or in an isolated form. The specification fails to disclose any functional assay that would enable one skilled in the art how to evaluate the biological activity of the regulatory element encoded by SEQ ID NO:7. In addition the specification fails to define the minimal structure or consensus core structure that defines the functional domain of the regulatory element present in the nucleic acid sequences of SEQ ID NO:7.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L. P. vs Faulding Inc.* 56 USPQ2d 1481 (CAFC 2000). In the instant case the specification only teaches nucleic acid sequence of SEQ ID NO:7 but fails to disclose any variant of SEQ ID NO:7 that has similar functional activity explicitly or implicitly as putatively claimed herein.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, e.g., *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021

Art Unit: 1636

(*Fed. Cir. 1991*). In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406*).

In the instant case the nucleic acid variants (as claimed) has been defined only by a statement of function that broadly encompasses regulation of transcriptional activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The variation as claimed also encompasses the conserved motifs, which are considered germane to the proposed functional activity. In addition the specification fails to define the minimal structure or consensus core structure that defines the functional domain of the regulatory element present in the nucleic acid sequences of SEQ ID NO:7. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Response to argument

The applicant argues that there is a clear description of SEQ ID NO:7, which has been structurally and functionally described. The applicant argues that a person of skill in the art would not expect substantial variation among species within the scope of the claims, because the hybridization conditions and percent identity set forth in the claim will yield structurally similar polynucleotides. The applicant argues that a representative species is disclosed, the claims are drawn to a genus that hybridizes with or has sequence identity to a given sequence, and activity is adequately described. The applicant argues that the polynucleotides of the instant invention have promoter activity,

Art Unit: 1636

and they have at least 90% identity to a reference structure. The applicant argues the instant application is in compliance with the written description requirement.

However, applicant's arguments are found NOT persuasive because the scope of invention as claimed encompasses any and all variants of SEQ ID NO:7, wherein the variant comprises a nucleic acid sequence which is 90% identical to SEQ ID NO:7 or any nucleic acid sequence that hybridizes SEQ ID NO:7. The specification fails to disclose any functional assay that would enable one skill in the art how to evaluate the biological activity of a regulatory element found in the SEQ ID NO:7 which is responsive to the presence of pyruvate. The earlier office action clearly states that the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, e.g., *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). In instant case the specification fails to identify the regulatory element found in the nucleotide sequence of SEQ ID NO:7. Therefore absent the knowledge of the minimal structure or consensus core structure that defines the functional domain of the regulatory element present in the nucleic acid sequences of SEQ ID NO:7, one skill in the art would conclude that applicant was not in the possession of the claimed genus which encompasses any and all variant of SEQ ID NO:7.

Claim 24 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 recites the limitation "said first nucleic acid". There is insufficient antecedent basis for this limitation in the claim (Note: claim 24 has not been canceled as asserted by the applicant)

Claim Rejections - 35 USC § 102

Claim 24 stand rejected under 35 U.S.C. 102(b) as being anticipated by Vyostskaia et al. Acc. No:AC000132, 1997.

The invention as claimed is drawn to a polynucleotide sequence comprising a sequence which comprises 20 contiguous nucleotides of a SEQ ID NO:7. Vyostskaia teaches an isolated polynucleotide sequence comprising a sequence comprising 23 contiguous nucleotides of a SEQ ID NO:7. Thus the cited art clearly anticipate the invention as claimed.

Response to argument

The applicant argues that the rejection is rendered moot by the cancellation of claim 24. However this is found not persuasive because claim 24 has not been canceled.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1636

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Sumesh Kaushal
Examiner GAU 1636



SUMESH KAUSHAL
PATENT EXAMINER